PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 01 September 2000 (01.09.00)	
International application No. PCT/IB99/02065	**Applicant's or agent's file reference** P020631WO
International filing date (day/month/year) 17 December 1999 (17.12.99)	**Priority date** (day/month/year) 18 December 1998 (18.12.98)
Applicant RATTI, Giulio	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

14 July 2000 (14.07.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia TEFY

Telephone No.: (41-22) 338.83.38

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TENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P020631WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB99/02065	17/12/1999	18/12/1998
International Patent Classification (IPC) or national classification and IPC C07K14/295		
Applicant CHIRON SPA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14/07/2000	29.03.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Buchet, A Telephone No. +49 89 2399 7401

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB99/02065

I. Basis of the rep rt

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-18 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 2-11 and 19-22 completely; 1, 12-18 and 23-24 partially.

because:

☒ the said international application, or the said claims Nos. 18 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 3-11 and 19-22 completely; 12-13, 15-18 and 23-24 partially are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1 and 3-24 partially; 2 completely.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	13, 15-18
	No:	Claims	1, 12, 14, 23-24
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1, 12-18, 23-24
Industrial applicability (IA)	Yes:	Claims	1, 12-17, 23-24
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
s e separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1: Electrophoresis
vol. 17, n° 1, 1996, pp 185-190
D2: WO 95 28487 A

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1) For the assessment of the present claim 18 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2) It is noted that the International Preliminary Examination Authority agrees with the non-unity of invention raised by the International Searching Authority: see reasoning in Form PCT/ISA/210 (extra sheets). The examination was then limited to the searched claims , i. e. claims 1 and 3-24 partially in so far as relating to the *Chlamydia trachomatis* protein 5.

3) The present application identifies a protein (protein 5) from *Chlamydia trachomatis* defined by its MW and pI, which is shown to immunologically react with some infected patient sera. However, the precise nature of this protein is not known since its amino acid sequence was not determined. Therefore, the subject-matter of claims 3-4, 20 and partially 23 relating to the protein sequence, of claims 5, 22 and partially 12-13, 15-18, 24 relating to specific antibodies and of claims 6-11, 19-21 and partially 12-13, 15-18, 24 relating to encoding DNA sequences, recombinant vectors and host cells, is not defined and is not supported by the description. In the absence of any characterising technical feature (Rule 6.3 PCT), no meaningful examination could be carried out on these aspects of the application.

The examination was restricted to claims 1, 14 and 12-13, 15-18, 23-24 partially in so far as relating to the *C. trachomatis* protein 5.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Novelty:

- D1 reports the isolation and partial identification of *C. trachomatis* proteins. In this aim, proteins were purified from elementary bodies of *C. trachomatis* strain L2 and separated by two dimensional gel electrophoresis on nonlinear wide-range immobilized pH gradients in the first dimension and polyacrylamide gradient gels in the second dimension. After silver staining (p 187, Fig. 1), *ca.* 600 spots could be reproducibly resolved. Using specific antibodies (p 188, Fig. 2) and N-terminal sequencing (p 189, Table 1), some of the proteins could be identified.

- As D1 and the present application use the same serovar and the same method of separation, it is expected that the claimed protein is efficiently isolated and detected in D1. Accordingly, a spot corresponding to a *C. trachomatis* protein having a pI of 5.09 and a MW of 36.6 could be located on Fig. 1. Therefore, the subject-matter of claim 1 is considered to be anticipated by D1. The same applies to claim 14 since the feature "for use as a chlamydial immunogen" is only interpreted as "suitable for" and does not confer any further characteristic to the known protein. The protein preparation of D1 corresponds to a composition as disclosed in claim 12. The gel obtained in D1 can be considered as a kit according to claim 24. Furthermore, the antibody solutions tested in D1 are biological samples and therefore, the immunoblot experiments performed in D1 anticipate the disclosure of the method claim 23.

- As a consequence, claims 1, 12, 14 and 23-24 do not fulfil the requirements of Article 33.2 PCT.

- However, D1 does not reveal that this particular protein reacts with a significant number of infected patient sera and then does not recommend it for diagnosis or

therapeutical purposes.

- Assuming that there is no other corresponding protein (see Item VIII-1) already described for its medical use or immunological properties, the subject matter of claims 13 and 15-18 is considered to be novel in the sense of Article 33.2 PCT.

2) Inventive step:

However, no inventive activity according to Article 33.3 PCT can be recognised for said claims:

- D2 reports a new purification process (claim 10) for the *C. trachomatis* pgp3 protein which gives rise to an efficient immunogen (claim 3). In this aim, the *pgp3* gene was placed under the pT7 promoter (claim 7) and the recombinant vector was transformed in *Escherichia coli* (claim 9). In response to IPTG, the protein of interest was overproduced and further purified by ion-exchange column chromatography (claim 12). The purified protein can be used as a medicament or a as a diagnostic reagent (claims 14-16).

- The technical problem to be solved by the present invention, as well as by D2 considered as the closest prior art, is the provision of alternative *C. trachomatis* antigens.

- The solution disclosed in the present application is the identification of a protein having a MW of 36, 6 kDa and a pI of 5,09.

- An efficient and reliable method for separating proteins from elementary bodies of *C. trachomatis* strain L2 being disclosed in D1, the skilled person would have tested the reactivity of the isolated proteins versus various sera from infected patients and selected those with the most interesting prevalence.

3) Claim 18 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

R Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, document D2 is not identified in the description. Furthermore, the relevant background art disclosed in the documents D1 and D2 is not mentioned therein.

Re Item VIII

Certain observations on the international application

1) A product should be defined by all its technical features (Article 6 PCT). This is not the case for the protein claimed in claim 1 or 14 which is defined by 2 parameters (MW and pI) which are not sufficient to differentiate it from the proteins disclosed in the prior art. Even the source of the protein does not necessary confer special features to it. Similarly, the immunogenic activity identified in the present application is merely considered as an inherent feature of the known protein and can not serve for establishing novelty. Only the characterisation of the protein by its sequence could fully define it and possibly confer novelty. However, in the present case, it can not be added in the claims since it was not disclosed in the application as filed.

2) It is noted that claim 1 should not refer to a figure but should explicitly give the value of pI and MW of the claimed protein.

3) The use of the claimed protein as a medicament or as a diagnostic reagent implies that the protein is isolated or even purified. However, the present application merely locates it on a gel. Therefore, the subject-matter of claims 13 and 15-18 lacks support in the description (Articles 5 and 6 PCT). This is particularly relevant in the light of D2 which reports inconsistent and unsatisfactory results of ELISA test obtained with pgp3 purified by electrophoresis on SDS-acrylamide gels (p 3, l 1-4).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
P020631WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB 99/02065	17/12/1999	18/12/1998
Applicant		
CHIRON S.P.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 11 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readble form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

CHLAMYDIA TRACHOMATIS ANTIGENS

5. With regard to the **abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 99/02065

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/295 C07K16/12 C12N15/31 C12N5/10 A61K38/16
A61K39/118 A61K39/395 A61K48/00 G01N33/569 C12P21/00
C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K G01N C12P C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	COLES A M ET AL: "Analysis of the human serological response to Chlamydia trachomatis 60-kDa proteins by two-dimensional electrophoresis and immunoblotting." FEMS MICROBIOLOGY LETTERS, (1991 JUL 1) 65 (3) 299-303., XP000864463	1,3-24
Y	the whole document	13-24
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 March 2000	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	ALCONADA RODRIG.., A

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BINI L ET AL: "Mapping of Chlamydia trachomatis proteins by immobiline-polyacrylamide two-dimensional electrophoresis: spot identification by N-terminal sequencing and immunoblotting." ELECTROPHORESIS, (1996 JAN) 17 (1) 185-90., XP000864457 cited in the application	1,3-24
Y	page 186, right-hand column, paragraph 3 -page 188, left-hand column, paragraph 1 page 189, right-hand column, paragraph 2 -page 190, left-hand column page 190, left-hand column, last paragraph figure 1 table 1 ---	13-24
X	GOSWAMI P C ET AL: "Extensive heterogeneity of the protein composition of Chlamydia trachomatis following serial passage in two different cell lines." JOURNAL OF GENERAL MICROBIOLOGY, (1990 AUG) 136 (PT 8) 1623-9., XP000864458	1,3-24
Y	table 1 figure 1 page 1624, right-hand column, last paragraph -page 1626, right-hand column, paragraph 2 ---	13-24
Y	WO 95 28487 A (BIOCINE SPA ;RATTI GIULIO (IT)) 26 October 1995 (1995-10-26) claims 1-16 page 14, line 25-30 page 37, line 19-26 page 38, line 33 -page 40, line 7 page 44, line 14 -page 59, line 20 ---	13-24
P,X	SANCHEZ-CAMPILLO M ET AL: "Identification of immunoreactive proteins of Chlamydia trachomatis by Western blot analysis of a two-dimensional electrophoresis map with patient sera." ELECTROPHORESIS, (1999 AUG) 20 (11) 2269-79., XP000900035 the whole document -----	1,3-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 99/02065

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9528487 A	26-10-1995	US 5629167 A	13-05-1997
		AU 2222795 A	10-11-1995
		CA 2188316 A	26-10-1995
		EP 0756630 A	05-02-1997
		JP 10503922 T	14-04-1998

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 99/02065

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 18 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1,3-24 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1,3-24 (partially)

A C.trachomatis protein having the MW and pI characteristics of protein 5, as set out in Table II on page 15 of the present application; an antibody against said protein, a nucleic acid encoding said protein, a vector comprising said nucleic acid, a host cell comprising said vector and a process of producing the protein by recombinant or chemical means; uses of the polypeptide, the polynucleotide and the antibody for treating or preventing a Chlamydia infection; and a process and a kit for the detection of the polypeptide, of the nucleic acid encoding said polypeptide, and of the antibody against said polypeptide.

2. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 6 as set out in Table II on page 15 of the present application.

3. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 7 as set out in Table II on page 15 of the present application.

4. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 8 as set out in Table II on page 15 of the present application.

5. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 9 as set out in Table II on page 15 of the present application.

6. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 11 as set out in Table II on page 15 of the present application.

7. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 13 as set out in Table II on page 15 of the present application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 14 as set out in Table II on page 15 of the present application.

9. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 15 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 15 as disclosed in Table III on page 16 of the present application.

10. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 16 as set out in Table II on page 15 of the present application.

11. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 17 as set out in Table II on page 15 of the present application.

12. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 18 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 18 as disclosed in Table III on page 16 of the present application.

13. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 20 as set out in Table II on page 15 of the present application.

14. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 21 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 21 as disclosed in Table III on page 16 of the present application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

15. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 22 as set out in Table II on page 15 of the present application.

16. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 23 as set out in Table II on page 15 of the present application.

17. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 24 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 24 as disclosed in Table III on page 16 of the present application.

18. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 25 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 25 as disclosed in Table III on page 16 of the present application.

19. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 26 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 26 as disclosed in Table III on page 16 of the present application.

20. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 27 as set out in Table II on page 15 of the present application.

21. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 28 as set out in Table II on page 15 of the present application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

22. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 29 as set out in Table II on page 15 of the present application.

23. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 30 as set out in Table II on page 15 of the present application.

24. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 31 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 31 as disclosed in Table III on page 16 of the present application.

25. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 32 as set out in Table II on page 15 of the present application.

26. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 33 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 33 as disclosed in Table III on page 16 of the present application.

27. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 34 as set out in Table II on page 15 of the present application.

28. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 35 as set out in Table II on page 15 of the present application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

29. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 36 as set out in Table II on page 15 of the present application.

30. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 37 as set out in Table II on page 15 of the present application.

31. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 38 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 38 as disclosed in Table III on page 16 of the present application.

32. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 39 as set out in Table II on page 15 of the present application.

33. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 40 as set out in Table II on page 15 of the present application.

34. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 41 as set out in Table II on page 15 of the present application.

35. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 42 as set out in Table II on page 15 of the present application.

36. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 43 as set out in Table II on page

15 of the present application.

37. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 44 as set out in Table II on page 15 of the present application.

38. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 45 as set out in Table II on page 15 of the present application.

39. Claims: 1-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 46 as set out in Table II on page 15 of the present application and having, in the L2 strain of C.trachomatis, the N-terminal sequence of protein 46 as disclosed in Table III on page 16 of the present application.

40. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 47 as set out in Table II on page 15 of the present application.

41. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 48 as set out in Table II on page 15 of the present application.

42. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 49 as set out in Table II on page 15 of the present application.

43. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 50 as set out in Table II on page 15 of the present application.

44. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 51 as set out in Table II on page 15 of the present application.

45. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 52 as set out in Table II on page 15 of the present application.

46. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 53 as set out in Table II on page 15 of the present application.

47. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 54 as set out in Table II on page 15 of the present application.

48. Claims: 1,3-24 (partially)

As subject 1, but comprising a protein having the MW and pI characteristics of protein 55 as set out in Table II on page 15 of the present application.

DUE: 5-1-01

PATENT COOPERATION TREATY

GTM, please

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
HALLYBONE, Huw George
CARPMAELS & RANSFORD
43 Bloomsbury Square
London WC1A 2RA
GRANDE BRETAGNE

SAW

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	05.10.2000
Applicant's or agent's file reference: P020631WO	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB99/02065	17/12/1999	18/12/1998

International Patent Classification (IPC) or both national classification and IPC
C07K14/295

Applicant
CHIRON SPA et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 18/04/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Buchet, A

Formalities officer (incl. extension of time limits)
Vullo, C
Telephone No. +49 89 2399 8061

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-18 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1, 12-18, 23-24, partially,

because:

☒ the said international application, or the said claims Nos. 18 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 3-11, 19-22 completely and 12-13, 15-18, 24 partially are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1 and 3-24 partially, 2 completely.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 12, 14, 23-24 (no)
Inventive step (IS)	Claims	1, 12-18, 23-24 (no)
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

D1: Electrophoresis
vol. 17, n° 1, 1996, pp 185-190
D2: WO 95 28487 A

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1)
- For the assessment of the present claim 18 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

- Claim 18 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

2) It is noted that the International Preliminary Examination Authority agrees with the non-unity of invention raised by the International Searching Authority: see reasoning in Form PCT/ISA/210 (extra sheets). The examination was then limited to the searched claims , i. e. claims 1 and 3-24 partially in so far as relating to the *Chlamydia trachomatis* protein 5.

3)
- The present application identifies a protein (protein 5) from *Chlamydia trachomatis* defined by its MW and pI, which is shown to immunologically react with some infected patient sera. However, the precise nature of this protein is not known since its amino

acid sequence was not determined. Therefore, the subject-matter of claims 3-4 and 20 relating to the protein sequence, of claims 5, 22 and partially 12-13, 15-18, 24 relating to specific antibodies and of claims 6-11, 19-21 and partially 12-13, 15-18, 24 relating to encoding DNA sequences, recombinant vectors and host cells, is not defined and is not supported by the description. In the absence of any characterising technical feature (Rule 6.3 PCT), no meaningful examination could be carried out on these aspects of the application.

- The examination was restricted to claims 1, 14 and 12-13, 15-18, 23-24 partially in so far as relating to the *C. trachomatis* protein 5.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Novelty:

- D1 reports the isolation and partial identification of *C. trachomatis* proteins. In this aim, proteins were purified from elementary bodies of *C. trachomatis* strain L2 and separated by two dimensional gel electrophoresis on nonlinear wide-range immobilized pH gradients in the first dimension and polyacrylamide gradient gels in the second dimension. After silver staining (p 187, Fig. 1), *ca.* 600 spots could be reproducibly resolved. Using specific antibodies (p 188, Fig. 2) and N-terminal sequencing (p 189, Table 1), some of the proteins could be identified.

- As D1 and the present application use the same serovar and the same method of separation, it is expected that the claimed protein is efficiently isolated and detected in D1. Accordingly, a spot corresponding to a *C. trachomatis* protein having a pI of 5.09 and a MW of 36.6 could be located on Fig. 1. Therefore, the subject-matter of claim 1 is considered to be anticipated by D1. The same applies to claim 14 since the feature "for use as a chlamydial immunogen" is only interpreted as "suitable for" and does not confer any further characteristic to the known protein. The protein preparation of D1 corresponds to a composition as disclosed in claim 12. The gel obtained in D1 can be considered as a kit according to claim 24. Furthermore, the antibody solutions tested in

D1 are biological samples and therefore, the immunoblot experiments performed in D1 anticipate the disclosure of the method claim 23.

- As a consequence, claims 1, 12, 14 and 23-24 do not fulfil the requirements of Article 33.2 PCT.

- However, D1 does not reveal that this particular protein reacts with a significant number of infected patient sera and then does not recommend it for diagnosis or therapeutical purposes.

- Assuming that there is no other corresponding protein (see Item VIII-1) already described for its medical use or immunological properties, the subject matter of claims 13 and 15-18 is considered to be novel in the sense of Article 33.2 PCT.

2) Inventive step:

However, no inventive activity (Article 33.3 PCT) can be recognised for said claims:

- D2 reports a new purification process (claim 10) for the *C. trachomatis* pgp3 protein which gives rise to an efficient immunogen (claim 3). In this aim, the *pgp3* gene was placed under the pT7 promoter (claim 7) and the recombinant vector was transformed in *Escherichia coli* (claim 9). In response to IPTG, the protein of interest was overproduced and further purified by ion-exchange column chromatography (claim 12). The purified protein can be used as a medicament or a as a diagnostic reagent (claims 14-16).

- The technical problem to be solved by the present invention, as well as by D2 considered as the closest prior art, is the provision of alternative *C. trachomatis* antigens.

- The solution disclosed in the present application is the identification of a protein having a MW of 36, 6 kDa and a pI of 5,09.

- An efficient and reliable method for separating proteins from elementary bodies of *C. trachomatis* strain L2 being disclosed in D1, the skilled person would have tested the

reactivity of the isolated proteins versus various sera from infected patients and selected those with the most interesting prevalence.

- In the absence of any indication that one of the features of claims 13 and 15-18 leads to an unexpected, advantageous effect of the entire scope of said claims, no inventive step (Article 33.3 PCT) can be recognised.

Re Item VII
Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, document D2 is not identified in the description. Furthermore, the relevant background art disclosed in the documents D1 and D2 is not mentioned therein.

Re Item VIII
Certain observations on the international application

1) A product should be defined by all its technical features (Article 6 PCT). This is not the case for the protein claimed in claim 1 or 14 which is defined by 2 parameters (MW and pI) which are not sufficient to differentiate it from the proteins disclosed in the prior art. Even the source of the protein does not necessary confer special features to it. Similarly, the immunogenic activity identified in the present application is merely considered as an inherent feature of the known protein and can not serve for establishing novelty. Only the characterisation of the protein by its sequence could fully define it and possibly confer novelty. However, in the present case, it can not be added in the claims since it was not disclosed in the application as filed.

2) It is noted that claim 1 should not refer to a figure but should explicitly give the value of pI and MW of the claimed protein.

3) The use of the claimed protein as a medicament or as a diagnostic reagent implies that the protein is isolated or even purified. However, the present application merely locates it on a gel. Therefore, the subject-matter of claims 13 and 15-18 lacks support

in the description (Articles 5 and 6 PCT). This is particularly relevant in the light of D2 which reports inconsistent and unsatisfactory results of ELISA test obtained with pgp3 purified by electrophoresis on SDS-acrylamide gels (p 3, l 1-4).

Concluding remarks:

When filing amended claims, the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 34(2)(b)PCT).

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).
If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.